General

Guideline Title

American College of Medical Genetics and Genomics guideline for the clinical evaluation and etiologic diagnosis of hearing loss.

Bibliographic Source(s)

Alford RL, Arnos KS, Fox M, Lin JW, Palmer CG, Pandya A, Rehm HL, Robin NH, Scott DA, Yoshinaga-Itano C, ACMG Working Group on Update of Genetics Evaluation Guidelines for the Etiologic Diagnosis [trunc], Professional Practice and Guidelines Committee. American College of Medical Genetics and Genomics guideline for the clinical evaluation and etiologic diagnosis of hearing loss. Genet Med. 2014 Apr;16(4):347-55. [114 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Genetic Evaluation of Congenital Hearing Loss Expert Panel. Genetics evaluation guidelines for the etiologic diagnosis of congenital hearing loss. American College of Medical Genetics and Genomics (ACMG) statement. Genet Med. 2002 May-Jun;4(3):162-71. [31 references]

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 14, 2016 – General anesthetic and sedation drugs : The U.S. Food and Drug Administration (FDA) is warning that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains. Consistent with animal studies, recent human studies suggest that a single, relatively short exposure to general anesthetic and sedation drugs in infants or toddlers is unlikely to have negative effects on behavior or learning. However, further research is needed to fully characterize how early life anesthetic exposure affects children's brain development.

Recommendations

Major Recommendations

1. All newborns and infants with confirmed hearing loss should undergo a comprehensive evaluation in which patient-focused medical and birth histories and a three-generation pedigree and family medical history are obtained, and a physical examination that focuses on dysmorphic physical findings is performed. Evaluation of children and young adults with hearing loss should follow a similar approach. Evaluation of deaf or hard-of-hearing adults should be customized based on the age of onset and other characteristics of the hearing loss (see Figure 1 in the original guideline document).
    - The medical and birth histories may be helpful in differentiating between acquired versus inherited causes of hearing loss. Elements of medical and birth histories focused on hearing loss include the following:
        - Prenatal history, including maternal infections (e.g., cytomegalovirus [CMV], rubella) and illnesses (e.g., syphilis), or medication or drug exposures (e.g., thalidomide, retinoic acid)
        - Neonatal history, including premature birth, low birth weight, birth hypoxia, hyperbilirubinemia, sepsis, and exposure to ototoxic medications
        - Postnatal history, including viral illnesses, bacterial meningitis, head trauma, noise exposure, and exposure to ototoxic medications
        - Audiometric assessment of the hearing loss, including sensorineural versus conductive or mixed hearing loss; age of onset; progressive, nonprogressive, or fluctuating nature of the hearing loss; laterality, symmetry, severity, and configuration of the hearing loss; and the presence or absence of vestibular dysfunction or auditory neuropathy
    - The pedigree and family medical history should focus on identifying the following:
        - First- and second-degree relatives with hearing loss or with features commonly associated with hearing loss (such as pigmentary, branchial, or renal anomalies) or sudden cardiac death
        - A pattern of inheritance
        - Ethnicity and country of origin
        - A common origin from ethnically or geographically isolated areas
        - Consanguinity
    - The physical examination should focus on dysmorphic and other physical findings such as the following:
        - Unusual facial appearance, with attention to asymmetry
        - Pigmentary anomalies
        - Neck, skin, facial, or ear anomalies
        - Neurological abnormalities
        - Balance disturbances
        - Skeletal abnormalities
        - Other unusual physical findings

2. For individuals with findings that suggest a syndromic genetic etiology for their hearing loss:
    - Pretest genetic counseling should be provided, and, with patient's informed consent, genetic testing, if available, should be ordered to confirm the diagnosis—this testing may include single-gene tests, hearing loss sequencing panels, whole-exome sequencing (WES), whole-genome sequencing (WGS), chromosome analysis, or microarray-based copy-number analysis, depending on clinical findings.
    - Appropriate studies should be undertaken to determine whether other organs are involved.
    - Appropriate near-term and long-term screening and management should be arranged, including referrals to specialists, as indicated by the associated manifestations of the particular syndrome.

3. For individuals lacking physical findings suggestive of a known syndrome and having medical and birth histories that do not suggest an environmental cause of hearing loss, a tiered diagnostic approach should be implemented.
    - Pretest genetic counseling should be provided, and, with patient's informed consent, genetic testing should be ordered.
        - Single-gene testing may be warranted in cases in which the medical or family history, or presentation of the hearing loss, suggests a specific etiology. For example, testing for mitochondrial deoxyribonucleic acid (DNA) mutations associated with aminoglycoside ototoxicity may be considered for individuals with a history of use of aminoglycoside antibiotics.
        - In the absence of any specific clinical indications and for singleton cases and cases with apparent autosomal recessive inheritance, the next step should be testing for DFNB1-related hearing loss (due to mutations in *GJB2* and adjacent deletions in *GJB6*).
        - If initial genetic testing is negative, genetic testing using gene panel tests, next-generation sequencing (NGS) technologies such as large sequencing panels targeted toward hearing loss–related genes, WES, or WGS may be considered. Because several tests are clinically available, the clinician must be aware of the genes included in the test (panel) chosen and the performance characteristics of the platform chosen, including coverage, analytic sensitivity, and what types of mutations will be detected. It should be noted that the cost of these new genetic sequencing technologies is decreasing so rapidly that a tiered approach to testing may soon no longer be cost effective. In particular, for large sequencing panels targeted toward hearing loss–related

genes, it may, in some cases, already be more cost effective to use NGS technologies as the initial test in the evaluation of hearing loss. However, issues related to genomic testing, such as the likelihood of incidental findings, will have to be addressed.
    - If genetic testing reveals mutation(s) in a hearing loss–related gene, mutation-specific genetic counseling should be provided, followed by appropriate medical evaluations and referrals.
    - If genetic testing fails to identify an etiology for a patient's hearing loss, the possibility of a genetic or acquired etiology remains. This point must be emphasized because it can be misunderstood by clinicians and by patients and their families. For interested patients and families, further genetic testing may be pursued on a research basis.
  - Temporal bone imaging by computed tomography or magnetic resonance imaging should be considered as a complement to genetic testing, particularly if the diagnosis remains unclear, if cochlear implantation is being considered, if auditory neuropathy is noted, in cases of progressive hearing loss, or if other clinical concerns exist. The anticipated clinical utility of imaging studies should be balanced against the risks associated with radiation exposure and sedation.
  - CMV testing should be done at the same time as genetic testing for infants with congenital hearing loss. For later-onset or progressive hearing loss, CMV testing can be obtained, but the likelihood that a positive test is due to postnatal exposure increases with age.

4. Referral to a multidisciplinary care center, when available, is recommended.
    - A team approach that includes otolaryngologists, clinical geneticists, genetic counselors, audiologists, speech and language specialists, early hearing intervention and family support specialists (which may include other individuals who are deaf or hard of hearing or other parents of deaf or hard-of-hearing children), and other appropriate specialists offers optimal opportunity to provide ongoing management and support of deaf and hard-of-hearing individuals and their families as their needs change over time.
    - For cases in which the genetic evaluation failed to identify an underlying cause, periodic follow-up care every 3 years with a geneticist may be appropriate for several reasons. First, subtle features of syndromic forms of hearing loss may not be apparent at birth or early in childhood but may appear as deaf or hard-of-hearing individuals grow into adulthood. These may prompt additional medical tests or referrals for specialty care. Second, follow-up visits offer the opportunity to inform individuals about new genetic tests that may have become available or changes in the interpretation of previous test results as medical knowledge advances. Finally, follow-up visits may also help identify clinical concerns unrelated to hearing loss, for which referral for specialty care may be appropriate (see Figure 1 in the original guideline document).

5. Regardless of whether genetic test results are positive, negative, or inconclusive, results should be communicated through the process of genetic counseling.

Clinical Algorithm(s)

An algorithm titled "Graphic Overview of Approaches to the Clinical Evaluation and Etiologic Diagnosis of Hearing Loss" is provided in the original guideline document.

Scope

Disease/Condition(s)

Hearing loss (inherited or acquired)

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Clinical Specialty

Family Practice

Medical Genetics

Otolaryngology

Pediatrics

Intended Users

Physician Assistants

Physicians

Guideline Objective(s)

- To provide information about the frequency, causes, and presentations of hearing loss
- To suggest approaches to the clinical evaluation of deaf and hard-of-hearing individuals aimed at identifying an etiologic diagnosis
- To provide informative and effective patient education and genetic counseling

Target Population

Deaf and hard-of-hearing individuals of any age

Interventions and Practices Considered

1. Patient history
    - Prenatal, neonatal, and postnatal history
    - Audiometric assessment of the hearing loss
    - Family pedigree (relatives with hearing loss, inheritance patterns, ethnicity, and consanguinity)
2. Physical examination focused on dysmorphic and other physical findings
3. Genetic testing
    - Hearing loss sequencing panels, whole-exome sequencing (WES), whole-genome sequencing (WGS), chromosome analysis, or microarray-based copy-number analysis
    - Single gene testing
    - DFNB1 testing
4. Genetic counseling (including mutation-specific genetic counseling)
5. Temporal bone imaging by computed tomography
6. Magnetic resonance imaging (MRI)
7. Cytomegalovirus (CMV) testing
8. Referral to a multidisciplinary care center
    - Team approach
    - Follow-up care

Major Outcomes Considered

- Sensitivity of diagnostic tests
- Clinical utility of genetic and non-genetic testing
- Prognostic accuracy
- Efficacy of patient education

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

A PubMed literature search was performed for the years 2011 to 2014. Additionally, Internet search engines were used to gather information from resources not contained within PubMed (resources used are cited in the original guideline document). Search terms included hearing loss, genetic, deafness, hereditary, and terms specific to individual genes including KCNQ4, ACTG1, SOX10, PAX3, SLC26A4, GJB2, specific syndromes such as Waardenburg syndrome type I, Pendred syndrome, Waardenburg syndrome type II, Usher syndrome types I and II, branchio-oto-renal, and specific ototoxic medications or laboratory methods.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published analyses were not reviewed.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations were based on a comprehensive review of published reports. In cases where the data did not appear conclusive, recommendations were based on the consensus opinion of the group.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate clinical evaluation and etiologic diagnosis of individuals with hearing loss

Potential Harms

The anticipated clinical utility of imaging studies (e.g., temporal bone imaging by computed tomography or magnetic resonance imaging) should be balanced against the risks associated with radiation exposure and sedation.

Qualifying Statements

Qualifying Statements

This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical services. Adherence to this guideline is completely voluntary and does not necessarily assure a successful medical outcome. This guideline should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that becomes available after that date. It also would be prudent to consider whether intellectual property interests may restrict the performance of certain tests and other procedures.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2002 May-Jun (revised 2014 Apr)

Guideline Developer(s)

American College of Medical Genetics and Genomics - Professional Association

Source(s) of Funding

American College of Medical Genetics and Genomics

Guideline Committee

American College of Medical Genetics and Genomics Working Group on Update of Genetics Evaluation Guidelines for the Etiologic Diagnosis of Congenital Hearing Loss

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Financial Disclosures/Conflicts of Interest

Christina G. Palmer has received grant support to develop educational materials on cancer for the Deaf community. Heidi L. Rehm is employed by a fee-for-service laboratory that offers diagnostic testing for hearing loss. The other authors declare no conflict of interest.

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Guideline Availability

Electronic copies: Available from the American College of Medical Genetics and Genomics (ACMG) Web site .

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 24, 2014. The information was verified by the guideline developer on August 1, 2014. This summary was updated by ECRI Institute on February 15, 2017 following the U.S. Food and Drug Administration advisory on general anesthetic and sedation drugs.

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